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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,486	08/31/2006	John S. Yu	22862-0003US1 / 67789-567	6180

26161 7590 01/27/2009

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EXAMINER	
JUEDES, AMY E	
ART UNIT	**PAPER NUMBER**
1644	

NOTIFICATION DATE	DELIVERY MODE
01/27/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/598,486	YU ET AL.	
	Examiner	Art Unit	
	AMY E. JUEDES	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/30/08, 12/21/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-11 are pending and are under examination.

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 10-11 recite the limitation "the disease condition" in line 1. There is insufficient antecedent basis for this limitation in the claim, or in independent claim 8.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method for treating cancer comprising administering tumor antigen loaded dendritic cells and a COX-2 inhibiting compound,

does not reasonably provide enablement for:

a method for treating a disease comprising administering dendritic cells and a COX-2 inhibiting compound.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by

the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, *in re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

"The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)" The MPEP further states that physiological activity can be considered inherently unpredictable.

The specification provides insufficient guidance to enable claims drawn to the method as broadly claimed. Note that the claims encompass treating any disease condition comprising administering a dendritic cell vaccine and a COX-2 inhibitor. Antigen loaded dendritic cell vaccines function to induce an antigen specific immune response, and have been used as a therapy treat cancer (see Song et al., 2004). Moreover, inhibition of COX-2 is known to enhance the stimulatory capacity of dendritic cells (see Harizi et al., 2002, J. Immunol). Thus, antigen loaded dendritic cell vaccines in combination with COX-2 inhibition might function to treat cancer. However, the instant claims encompass treating any disease condition, which might include treating Alzheimer's disease, autoimmune disease, cardiovascular disease, depression etc. The ability of a single treatment regimen to be effective for such a broad range of diseases with different etiologies and pathological mechanisms is highly unpredictable. For example, it is unclear how a DC vaccination strategy that functions to induce an immune response would be useful for treating conditions such as depression, which do not have an immune mediated mechanism. Likewise, the ability of DC vaccines that induce antigen specific immune responses to treat autoimmune disease is highly unpredictable,

since the goal of autoimmune treatments involves suppression of antigen specific immune response. Moreover, the instant claims encompass treating diseases such as cancer by administering any DC vaccine. Successful DC vaccination for treating cancer requires induction of a tumor specific T cell response. In fact, a critical factor in the success of DC vaccines for treating cancer is the choice of tumor antigen for DC loading (see Song et al., page 48-49 in particular). However, the instant claims do not require administering a tumor antigen loaded dendritic cell, and encompass administration of unloaded dendritic cells. Based on the state of the art, it would be highly unpredictable whether an unloaded dendritic cell could function to induce tumor specific T cells and treat cancer.

Thus, based on the unpredictability of the art and the breadth of the claims, the instant specification must provide a sufficient and enabling disclosure commensurate in scope with the instant claims. The instant specification demonstrates that inhibition of COX-2 in vitro enhances the TH1 inducing potential of dendritic cells co-cultured with tumor cells. However, no examples are provided that demonstrate that dendritic cell vaccines in combination with COX-2 inhibitors would be effective for treating diseases other than cancer. Additionally, no examples are provided that unloaded dendritic cells in combination with COX-2 inhibitors can function to treat cancer. Accordingly, the method as broadly claimed must be considered highly unpredictable. Given said unpredictability, the method of the instant claims must be considered to require undue experimentation.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-5 and 8-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zitvogel et al., 1996 (of record), in view of Harizi et al., March 2002, and Rioux et al., 1998.

Zitvogel et al. teach that tumor peptide pulsed dendritic cells can be administered as a vaccine to induce tumor specific T cells for treating cancer. Zitvogel et al. also teach that the ability of the dendritic cells to induce tumor protection is critically dependent on the production of IL-12 and the induction of a Th1 type immune response (see page 95 in particular). Zitvogel et al. also teach administering 3-5 x 10^5 dendritic cells in each vaccination (see page 89 in particular).

Zitvogel et al. do not teach administering a COX-2 inhibitor.

Rioux et al. teach administering COX-2 inhibitors, including NS-398, results in reduced tumorigenesis and reduced tumor volume (see page 5359 in particular). Rioux et al. also teach administering the COX-2 inhibitors at a range of doses, including at a dose of 588 mg/kg of the diet. Rioux et al. teach that average consumption of the food per day is 2.38 g/day, which correlates to an effective dose of approximately 1.4 mg (see page 5357 in particular). Rioux et al. also teach that inhibition of COX-2 decreases the level of PGE-2 (i.e. decreased PGE-2 activity, see page 5355 in particular).

Harizi et al. teach that COX-2 inhibitors such as NS-398 increase the IL-12 production and the stimulatory capacity of dendritic cells (see page 2255 in particular). Harizi et al. also teach that the mechanism of increased dendritic cell stimulatory capacity is by inhibition of PGE2.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to administer a COX-2 inhibitor such as NS-398,

as taught by Rioux et al., in the method of treating cancer by tumor antigen pulsed dendritic cell vaccination of Zitvogel. The ordinary artisan would have been motivated to do so and have a reasonable expectation of success, since Rioux et al. teach that COX-2 inhibitors reduce tumor volume and inhibit tumorigenesis. Additionally, the ordinary artisan would have been further motivated to administer the COX-2 inhibitor along with a dendritic cell vaccine, since Harizi et al. teach that inhibition of COX-2 increases IL-12 production and stimulatory capacity of dendritic cells, and Zitvogel et al. teach that IL-12 production by dendritic cells is crucial to the induction of a tumor protective Th1 immune response.

6. Claims 6-7 and 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zitvogel et al., Rioux et al., and Harizi et al., as applied to claims 1-5 and 8-9 above, and further in view of Yu et al., 2001 (of record).

The combined teachings of Zitvogel et al., Rioux et al., and Harizi et al. are discussed above.

They do not teach treating glioma.

Yu et al. teach that tumor peptide pulsed dendritic cells are safe and effective for inducing tumor specific T cells for the treatment of glioma (i.e. brain cancer, see page 846 in particular).

Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the cancer treatment method made obvious by Zitvogel et al., Rioux et al., and Harizi et al., to treat glioma as taught by Yu et al. One of ordinary skill in the art at the time the invention was made would have been motivated to do so, and have a reasonable expectation of success, since Yu et al. teach that tumor peptide pulsed dendritic cells are safe and effective for inducing tumor specific T cells for the treatment of glioma.

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes whose telephone number is 571-272-4471. The examiner can normally be reached on 7am to 3:30pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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